

## REMARKS

### *Status of the Claims*

Claims 1-13, 16-18, and 21-42 are pending.<sup>1</sup> Claims 16-18, 21, 23, 25, and 27-33 were previously withdrawn from consideration as being drawn to a non-elected invention. Claims 14-15 and 19-20 were previously canceled. By virtue of this response, claims 1-5, 7-8, 10, 22, 24, 26, 36, 38, 40, and 42 have been canceled, claims 6, 9, 11, 34, 35, 39, and 41 have been amended, and new claims 43-50 have been added. Accordingly, claims 6, 9, 11-13, 34-35, 37, 39, 41, and 43-50 are currently under examination.

The claim amendments and new claims are supported by the specification as follows: The amendments to claim 6, and new claim 50, are supported for example on page 33, lines 26-30, page 35, lines 18-24, page 36, lines 5-13, page 41, lines 25-26, page 7, lines 23-30, page 38, lines 22-24, and on page 42, lines 11-13. The amendment to claim 9 is supported for example on page 8, lines 14-15. The amendment to claim 11 is supported for example on page 10, lines 15-20. The amendment to claim 34 is supported for example on page 35, lines 18-24. The amendment to claim 35 is supported for example on page 9, lines 9-10. The amendment to claim 39 is supported for example on page 9, lines 11-14. The amendment to claim 41 is supported for example on page 8, lines 14-15 and on page 9, lines 9-10. New claims 43 and 44 are supported for example on page 36, lines 5-13 and in Figure 12 (peptide 4). New claims 45 and 49 are supported for example in Example 6 (page 36, line 28 - page 37, line 26). New claims 46-48 are supported for example on page 37, lines 16-26. The amendments to the specification were made merely to identify the sequences depicted in the figures with their corresponding SEQ ID NOs. Thus, no new matter has been added by the foregoing amendments.

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<sup>1</sup> Applicant respectfully notes that the Office Action Summary incorrectly lists claims 1-13, 22, 24, 26, and 34-42 as pending and incorrectly fails to note that claims 16-18, 21, 23, 25; and 27-33 were previously withdrawn from consideration.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned **“VERSION WITH MARKINGS TO SHOW CHANGES MADE.”**

With respect to any claim amendments or cancellations, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover has not acquiesced to any rejections and/or objections made by the Patent Office. Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicant has carefully considered the points raised in the Office Action and believes that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance, which is respectfully requested.

***Notice to Comply with Sequence Disclosure Requirements***

In response to the Notice to Comply with sequence disclosure requirements, Applicants are submitting a new Sequence Listing concurrently with this Request for Continued Examination. Further, Applicants have amended the claims to include SEQ ID NOs, as required in the Notice to Comply.

It has come to Applicant's attention that there is a clerical error in the sequence represented as peptide 4 in Figure 12. The terminal amino acid in this sequence should be Glycine (G) rather than Serine (S). Applicants are submitting a corrected figure herewith, along with a copy of the original figure that includes changes indicated in red ink in accordance with MPEP § 608.02(p). SEQ ID NO:39 of the sequence listing depicted the correct sequence. Therefore, no new matter is added by the correction to the figure.

It has also come to Applicant's attention that a clerical error was included in SEQ ID NO:19 in the Sequence Listing filed on April 7, 2000. In particular, an Asparagine (Asn) residue should have been included at position 28 of SEQ ID NO:19. This error has been corrected in the Sequence Listing that is being submitted concurrently with this response. Figure 5 of the

application as filed (Fragment 1) contained the correct amino acid sequence corresponding to SEQ ID NO: 19. Therefore, no new matter is added by the correction to the sequence listing.

***Rejection Under 35 U.S.C. § 112, second paragraph***

A. Claims 1, 5, and 6 are rejected as allegedly vague and indefinite due to recitation of the phrase “consisting essentially of.” The claims as amended no longer contain this phrase, rendering the rejection moot.

B. Claim 2 is rejected as allegedly vague and indefinite due to recitation of the phrase “mutants and variants thereof.” The claims as amended no longer contain this phrase, rendering the rejection moot.

C. Claims 1 and 6 are rejected as allegedly vague and indefinite due to recitation of the phrase “a structural homologue thereof.” The claims as amended no longer contain this phrase, rendering the rejection moot.

D. Claims 22 and 24 are rejected as allegedly vague and indefinite due to recitation of the terms “a peptide” and “a peptidomimetic compound.” The claims as amended no longer contain this phrase, rendering the rejection moot.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

***Claim Rejection Under 35 U.S.C. § 112, first paragraph***

Claims 1-13, 22, 24, 26 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. Applicants respectfully traverse this rejection.

Amended claim 6 recites a compound comprising a contiguous sequence of amino acids within the sequence representing residues 149-197 of the RSV G protein, wherein more than one of cysteines 173, 176, 182, and 186 is absent or blocked and the compound is not glycosylated, and wherein the compound has the ability to inhibit infectivity of RSV. Methods for making peptides of the invention and using them to inhibit infectivity of RSV are disclosed in the

specification. The specification provides sufficient guidance to enable one of skill in the art to make and use the claimed invention.

The specification discloses methods of producing peptides of the invention by both proteolytic digestion (*e.g.*, page 17, line 11 - page 18, line 5) and solid phase synthesis (*e.g.*, page 18, line 8 - page 19, line 16). Further, the specification discloses that examples of suitable assays for measuring inhibition of infectivity include inhibition of cytopathic effect or inhibition of viral proliferation (page 8, lines 4-6), and discloses methods for performing such assays, along with experimental data that shows that compounds of the invention are able to bind to RSV susceptible cells (HEp-2 cells) and inhibit the cytopathic effect of RSV on these cells. For example, Examples 4 and 5 disclose experiments in which binding of compounds of the invention to HEp-2 cells was observed. Fluorescent derivatives of the compounds were used, and binding was visualized using flow cytometry and confocal scanning microscopy. Example 6 discloses data showing the ability of peptide compounds of the invention to inhibit the cytopathic effect (cpe) of the A2 strain of RSV on HEp-2 cells in comparison with control cells infected with virus in the absence of the compounds. Peptide derivatives 1-4, depicted in Figure 12, were found to inhibit the cpe of the A2 strain with IC50 values ranging from 5-50 $\mu$ M. Thus, the antiviral activity exhibited in these experiments demonstrates that the claimed compounds are able to inhibit infectivity of RSV.

In conclusion, the specification provides adequate guidance to enable one of skill in the make and use the claimed invention. In view of the disclosed methods and working examples in the specification, it would not require undue experimentation for one of skill in the art to practice the invention.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

***Rejection Under 35 U.S.C. § 102***

Claims 1-6, 8, 10, 22 and 24 are rejected under 35 U.S.C. § 102(b)<sup>2</sup> as allegedly anticipated by Alkerlind-Stopner et al. (*J. Virol.*, 1990, 64:5143-5148). Applicants respectfully traverse this rejection.

In order for a reference to anticipate, each and every element of the claimed invention must be disclosed in the reference. Claim 6 as amended recites that more than one of cysteines 173, 167, 182, and 186 is absent or blocked. Alkerlind-Stopner et al. does not disclose the claimed element of absence or blockage of more than one of cysteines 173, 176, 182, and 186 of RSV G protein. Further, this reference does not teach the ability of such peptides to inhibit infectivity of RSV as claimed. Therefore, Alkerlind-Stopner does not anticipate the claimed invention.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

***Rejection Under 35 U.S.C. § 103***

Claims 1-13, 22 and 24 are rejected under 35 U.S.C. § 103(a)<sup>3</sup> as allegedly obvious in view of Alkerlind-Stopner et al. (*J. Virol.*, 1990, 64: 5143-5148 and Guichard (*PNAS*, 1994, 91:9765-9769). Applicants respectfully traverse this rejection.

A *prima facie* case for obviousness includes, *inter alia*, a requirement that references, when combined, must teach or suggest all the limitations of a claimed invention (MPEP § 2142). Alkerlind-Stopner et al., in combination with Guichard, does not teach or suggest all of the limitations of the present invention as claimed. As discussed above, Alkerlind-Stopner does not teach RSV G protein peptides in which more than one of cysteines 173, 176, 182 and 186 is

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<sup>2</sup> The Office Action states that the rejection is under 35 U.S.C. “§112(e),” but the rejection appears to be under 35 U.S.C. § 102(b).

<sup>3</sup> The Office Action states that the rejection is under 35 U.S.C. “§112(e),” but the rejection appears to be under 35 U.S.C. § 103(a).

absent or blocked. Guichard, which discloses retro-inverso-peptidomimetic analogues of natural L-peptides, does not supply this missing element. The combination of Alkerlind-Stopner with Guichard would not allow one of skill in the art to arrive at the claimed invention, because the combination does not teach or suggest a compound comprising a contiguous sequence of amino acids within the sequence representing residues 149-197 of RSV G protein, wherein more than one of cysteines 173, 176, 182 and 186 is absent or blocked, and wherein the compound has the ability to inhibit infectivity of RSV. There is no disclosure in either of the references that the claimed peptides could or would inhibit infectivity of RSV in the absence or blockage of more than one cysteine residue. In fact, Alkerlind-Stopner et al. teaches away from the concept that these peptides could retain activity in the absence or blockage of more than one cysteine residue. The reference states that “[t]he three cysteines in positions 176, 182, and 186 play a *critical role* in maintenance of the antigenic reactivity of peptide 12. Deletion of any one of these three cysteines reduced the reactivity of peptide 12G(A) and 12G(B) nearly completely in reactions with MAbs.” (p. 5147, emphasis added) In view of this statement, one of skill in the art would not expect the claimed peptides to retain activity in the absence or blockage of more than one cysteine residue. Therefore, the claimed invention is not obvious over the combination of the two cited references.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

## CONCLUSION

Applicant has, by way of the amendments and remarks presented herein, removed the issues for the rejections and addressed all issues that were raised in the outstanding Office Action. Accordingly, reconsideration and allowance of the pending claims are respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 273402004000.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

### **In the Specification**

Please replace the paragraph beginning on page 11, line 18, with the following rewritten paragraph:

Figure 2 (SEQ ID NOs:1-18) shows the amino acid sequence encompassing residues 149-197 of the G proteins of variants of different subtypes of RSV. Sequences 1-15 are human RSV strains, sequence 1 is that of the A2 strain of the A subtype (Satake *et al*, 1985; Wertz *et al*, 1985), sequence 2 is the Long A strain of the A subtype (Johnson *et al*, 1987), and sequences 3-8 are natural variants of the A subtype isolated in the same locality in a single year (Cane *et al*, 1991; Sullender *et al*, 1990; Sullender *et al*, 1991). Sequence 16 is that of Bovine RSV (Lerch *et al*, 1990). Sequences 17 and 18 are variants of human RSV, R10c/1 and R10c/10, which were generated by propagation of the Long A strain in the presence of a monoclonal antibody directed to the cysteine-containing constant region of the ectodomain of the G protein (Rueda *et al*, 1994);

Please replace the paragraph beginning on page 12, line 20, with the following rewritten paragraph:

Figure 5 (SEQ ID NOs: 19-29) shows the proposed identities of peptide fragments detected by MALDI-TOF-MS in various digests and HPLC fractions. Theoretical  $m/z$  values corresponding to the proposed fragments identities are presented next to the corresponding sequence. All  $m/z$  values are for the oxidized sequences, except for fragments 1R, 2R, and 3R, which are for reduced forms of these sequences;

Please replace the paragraph beginning on page 13, line 25, with the following rewritten paragraph:

Figure 10 (SEQ ID NOs: 30-31) illustrates the proposed fragmentation pattern of peptic fragment 2 based on data from Figure 9A.

Please replace the paragraph beginning on page 13, line 27, with the following rewritten paragraph:

Figure 11 (SEQ ID NOs: 32-35) shows the sequences of residues 149-197 from human, bovine, and ovine RSV G protein, indicating the features which are common to all strains.

Please replace the paragraph beginning on page 13, line 30, with the following rewritten paragraph:

Figure 12 (SEQ ID NOs: 36-44) shows the sequences of the peptide derivatives described herein.

#### **In the Claims**

6. (Twice Amended)            A compound [consisting essentially of] comprising a contiguous sequence of amino acids within the sequence representing residues 149-197 of the G protein of respiratory syncytial virus (RSV), [or a structural homologue thereof,] wherein [at least one] more than one of cysteines 173, 176, 182 and 186 is absent or blocked, [and in which] wherein said compound is not glycosylated, and wherein said compound has the ability to inhibit infectivity of RSV.

9. (Thrice Amended)            A compound according to claim [1] 6, wherein one or more amino acids is replaced by its corresponding D-amino acid.

11. (Thrice Amended) A compound according to claim [1] 6, wherein the compound is labelled with a detectable marker.

34. (Once Amended) A compound according to claim [1] 6, wherein the contiguous sequence represents residues 149 to 177 of the G protein of [respiratory syncytial virus] RSV.

35. (Once Amended) A diagnostic composition comprising a compound according to claim [1] 6, together with an acceptable carrier].

39. (Once Amended) A composition comprising a compound according to claim [1] 6, together with a pharmaceutically acceptable carrier.

41. (Once Amended) A composition comprising a compound according to claim [1] 6, wherein one or more amino acids is replaced by its corresponding D-amino acid.